REMARKS

The Examiner's Office Action mailed August 3, 2010, which rejected all pending claims, has been reviewed. Reconsideration in view of the foregoing amendments and remarks is respectfully requested. Moreover, Applicants have reviewed the Office Action of August 3, 2010, and submit that the following amendments and remarks are responsive to all points raised therein. Applicants believe that currently pending claims 1 and 3 are now in form for allowance.

Status of Claims

Claims 1 and 3 are pending in the application. No new matter has been added.

Objection to the Specification

Applicants have amended the specification. Applicants note that Artificial Beef Flavor is not a trademark, if that is what the examiner is referring to. As such, applicants request that this objection be withdrawn.

Rejection of Claims 1 and 3 under 35 USC § 103(a)

Reconsideration is requested of the rejection of claims 1 and 3under §103(a) as being unpatentable over Faour et al. (US 6004582) in view of Thombre (US Patent Application Publication 20030175326), Gennaro, 1990, and Federal Registry, 1997 (vol. 62(139) 38906-38907) as modified by Federal Registry, 1999 (vol. 64(171) 48295).

The present invention was developed to enable the administration of a bitter substance, enrofloxacin, to companion animals as tablets by addition of flavorings without impairing the mechanical properties of the tablets.

"Section 103 forbids issuance of a patent when 'the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." KSR Int'l Co. v. Teleflex Inc., 127 S.Ct. 1727, 1734, 82 USPQ2d 1385,

1391 (2007). The question of obviousness is resolved on the basis of underlying factual determinations including (1) the scope and content of the prior art, (2) any differences between the claimed subject matter and the prior art, (3) the level of skill in the art, and (4) where in evidence, so-called secondary considerations. Graham v. John Deere Co., 383 U.S. 1, 17-18, 148 USPQ 459, 467 (1966). See also KSR, 127 S.Ct. at 1734, 82 USPQ2d at 1391 ("While the sequence of these questions might be recorded in any particular case, the [Graham] factors continue to define the inquiry that controls.")

The Supreme Court described three cases that were illustrative of obviousness when the combination of familiar elements is done by known methods. The Supreme Court also stated that "[f]ollowing these principles may be more difficult in other cases than it is here because the claimed subject matter may involve more than the simple substitution of one known element for another or the mere application of a known technique to a piece of prior art ready for the improvement." Id. at 1740, 82 USPQ2d at 1395. The Court explained, "[o]ften, it will be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue." Id. At 1740-41, 82 USPQ2d at 1396. The court noted that "[t]o facilitate review, this analysis should be made explicit." Id., citing In re Kahn, F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006) ("[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness").

The KSR Court also recognized that "[w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp." In such circumstances, "the fact

that a combination was obvious to try might show that it was obvious under § 103."

Applicants submit this is not the case here. The Examiner proposes that the Faour reference teaches a formulation that includes a therapeutic agent, microcrystalline cellulose, and lactose (Example 2). The Examiner also notes that Faour teaches a number of agents including antibacterial agents, one of which is enrofloxacin, the addition of flavoring to the formulation, and then states that it would be obvious to someone in the art to optimize the concentrations of the ingredients in the formulation.

Applicants submit there are several mistakes with the Examiner's reasoning. First, Faour teaches a multi-layered osmotic tablet, whose primary purpose is the delivery of an active in a controlled release manner. Each layer of the multi-layered tablet is prepared in a different way to create different layers that release the active from the tablet. Someone skilled in the art developing an uncoated conventional tablet that masks bitter taste would not look to a controlled release formulation that requires multi-layers for controlled release. These are different problems.

Second, the Examiner picks and chooses the combination of ingredients from the Example and the specification to come up with the present invention. The Examiner cites Example 2 to show the combination of the agent, microcrystalline cellulose and lactose and he also states that Faour teaches a compressed formulation which would be an uncoated tablet. One skilled in the art would read the specification and Examples in more detail and not come to the conclusion the Examiner has. In particular, if one looks at Example 2 in more detail, there is a first layer of the osmotic tablet that includes d-pseudoephedrine hydrochloride, sodium chloride, microcrystalline cellulose, poly(vinylpyrrolidone), poly(ethylene glycol), ethyl alcohol, water, silicon dioxide, and magnesium stearate. The first layer is called the uncoated core by Faour. This uncoated core is then coated with a solution of cellulose acetate and polyethylene glycol in a mixture of methylene chloride and methanol for form a semipermeable membrane coated core. This coated core is perforated with a laser to form a

semipermeable coat. This perforated core is then covered with a suspension of Kollidon VA64, titanium dioxide, talk, and Punzo 4R Aluminum Lake in isopropyl alcohol to form cores coated with the polymer coat. The coated cores are subjected to a coating process through compression with a granulate. This granulate includes loratidine, lactose monohydrate, microcrystalline cellulose, maize starch, povidone, polyethylene glycol, colloidal silicon dioxide, and magnesium stearate. Finally a finishing coat is applied over this granulate coating. Looking at this example, the combination which the Examiner cites agent, lactose, and microcrystalline cellulose is actually a granulate used as a coating layer for a tablet, not a granulate that one would use as an uncoated tablet. The Examiner is assuming someone skilled in the art would take a huge leap from a coating to an uncoated tablet without any other evidence provided to make such a leap other than applicant's invention.

Third, the Examiner states that it would be obvious for someone skilled in the art to pick enrofloxacin from all the agents described in Faour since one is picking from a limited group of actives. Although the KSR court stated that if there is a "finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp," this is not the case here. As in the Ortho-McNeil Pharmaceutical, Inc case, wherein the court that stated that [t]he record ...does not present a finite (and small in the context of the art) number of options easily traversed to show obviousness..."[1] there are not few actives suggested in the Faour patent. Instead, there are hundreds of compounds of different classes and different properties. One skilled in the art would not even likely start with the compound selected by the inventor. Second, the person skilled in the art would have to have some reason to produce a standard release tablet vs a controlled release tablet described in Faour. Finally, the person skilled in the art would have to have decided to test the uncoated tablet rather than the multi-layered tablet of Faour. As stated further by the Eisai court, "[t]o the extent an art is unpredictable, as the chemical arts often are, KSR's focus on these "identified,

[1] Ortho-McNeil Pharmaceutical, Inc. v. Mylan Labs, Inc., 520 F.3d 1358, 1364 (Fed Cir 2008)

predictable solutions, may present a difficult hurdle because potential solutions are less likely to be genuinely predictable."[2]

The Examiner goes on to acknowledge that the Faour patent does not expressly teach meat flavoring or the claimed concentration of lactose and meat flavoring. These deficiencies, the Examiner proposes, are cured by the teachings of Thrombe and Gennaro, 1990 and FR 1997 as modified by FR 1999.

Applicants once submit there are some errors in the Examiner's rationale. Even if someone started with the Faour reference, which applicants submit that one skilled in the art would not for all the reasons detailed above, the combination with Thombre, Gennaro, FR 1997 and FR 199 would not yield the present invention. First, like Faour, Thombre teaches a coated tablet, whose primary purpose is the delivery of an active in a controlled release manner. The tablet is prepared in such a way and with a coating release the active from the tablet in a controlled manner. Someone skilled in the art developing an uncoated conventional tablet that masks bitter taste would not look to a controlled release formulation that requires coatings for controlled release. These are different problems. A controlled release tablet behaves differently than a conventional tablet. In particular, the amount of bitter drug release per unit of time is much less with a controlled release formulation than that of a conventional uncoated tablet. When the tablet is masticated by the animal, the bitterness is extremely worse with a conventional tablet compared to the formulation envisioned by Thrombe. It is like comparing apples to oranges for a person of skill in the art.

Second, the Examiner cites to example 1 to show that Thrombe has working examples of formulations preferred by canines comprising artificial flavor, however, this Example would not lead someone skilled in the art to the present invention. Example 1 refers to the acceptance of dogs of: (1) an unflavored placebo tablet, (2) flavored placebo tablets, and (3) unflavored placebo tablets with Bitrex. A person of ordinary skill in the art of course would have looked for the acceptance data of a flavored tablet with Bitrex which is

[2] Eisai Co. Ltd v. Dr. Reddy's Labs, Ltd., 533 F.3d 1353, 1359 (Fed Cir 2008)

missing. The only data provided is a flavored placebo tablet, not one with an ingredient that is bitter.

The combination of Faour and Thombre may lead someone skilled in the art to a multi-layered osmotic tablet with flavor but not a conventional uncoated tablet as suggested by the examiner, and definitely not an uncoated tablet of the present invention.

The Examiner combines the FR 1997 as modified by FR 1999 to support the teaching that enrofloxacin tablets existed and were administered to dogs. However, the combination of Faour, Thombre, and FR 1997 as modified by FR 1999 once again is flawed for all the reasons above. Finally, once skilled in the art combining all these references may end up with a multi-layered osmotic enrofloxacin tablet with flavor but not a conventional uncoated tablet as suggested by the examiner, and definitely not an uncoated enrofloxacin tablet of the present invention.

The Examiner uses the Gennaro reference to teach that lactose and microcrystalline cellulose are diluents used in tablet formulation and that 5-15% of microcrystalline cellulose is used as an excipient in direct compression formulas. In addition to the arguments already provided, Applicants submit the following. The Gennaro chapter is a very broad chapter typically used in curriculum of pharmacy courses worldwide. It suggests not only lactose as a filler but several others as well. It does not teach the developer which form of lactose should be chosen for applicants' specific goal especially when high percent of bitter and crystalline active is present in the formulation. It is in fact quite common in the pharmaceutical development of solid dosage forms to use maize starch as a filler. Indeed, often a majority of scientists use maize starch over lactose (since the latter is available in different forms and crystallizes out when it comes into contact with moisture) as a diluent. Maize is also considered as having an advantage over lactose due to the fact that is acts as a diluent and also as a disintegrant, it is water soluble when a drug is poorly soluble in water. Therefore, surprisingly the tablets prepared by applicant with maize starch (1164) are very inferior as compared to a formulation (1165) containing lactose and

microcrystalline cellulose (See declaration and example submitted previously). Such a dramatic improvement in tablet crushing strength and almost negligible friability was a surprise to Applicants specially by including 10% microcrystalline cellulose and 35% lactose monohydrate in the formulation. The tablet (1165) did disintegrate like any other conventional tablet.

The Examiner further quotes the Lewis reference. Applicants submit that the Examiner is correct that Lewis teaches maize starch is expected to give softer tablets and poor flow when the concentration in the formulation is 60% and above. In the present invention, Applicants found that even at levels below 60% maize starch could give softer tablets which are not acceptable.

As such, Applicant submit that claims 1 and 3 are patentable over Faour et al. in view of Thombre, Gennaro, and Federal Registry, 1997 as modified by Federal Registry, 1999.

Rejection of Claims 1 and 3 under 35 USC § 103(a)

Reconsideration is requested of the rejection of claims 1 and 3 under §103(a) as being unpatentable over Gerolymatos (US 5980914), Faour et al. (US 6004582) in view of Thombre (US Patent Application Publication 20030175326), Gennaro, 1990, and Federal Registry, 1997 (vol. 62(139) 38906-38907) as modified by Federal Registry, 1999 (vol. 64(171) 48295).

The Gerolymatos patent teaches formulations that include clioquinol. Clioquinol is an antifungal and antiprotozoal drug. The Examiner submits that he Gerolymatos patent teaches an uncoated formulation that includes an antimicrobial, microcrystalline cellulose, povidone, starch and/or lactose, maize starch, magnesium stearate, colloidal silicon dioxide, and a sweetening or flavoring. In addition, the Examiner states that the excipients recited are considered functional equivalents as noted where the Gerolymatos patent recites functions the given excipients. The Examiner then proceeds to state that although the Gerolymatos patent do not teach the percentages of each compound, a meat flavoring, or the concentrations of lactose and meat flavor this deficiency is cured by Faour, Thombre, Gennaro, and FR.

Applicants respectfully disagree. First, Gerolymatos teaches a substance that is not bitter. The addition of sweetening or flavoring agents is optional as this drug is meant for people rather than animals. Clioquinol is not a bitter substance, whereas the active of the present invention, enrofloxacin, is. Gerolymatos desires to formulate clioquinol to remove or alleviate some of the side effects of clioquinol. The side effects Gerolymatos is trying to avoid with his formulation are the occurrence of subacute myelo-optico-neurophathy (SMON). This is done by administering vitamin B_{12} in combination with clioquinol so that the vitamin B_{12} binds the byproduct of clioquinol and preventing this harmful effect. The purpose of Gerolymatos is not to produce a palatable uncoated tablet that contains a bitter active. Someone skilled in the art would not look to Gerolymatos for a solution to the problem presented as the starting point of the present invention. Applicants submit that the Examiner is using Applicants' invention as a road map to come up with a combination of multiple references and state Applicants' invention is obvious.

Applicants have presented all of the arguments for Faour, Thombre, Gennaro, and FR above. The addition of Gerolymatos does not change the analysis above. As such, Applicant submit that claims 1 and 3 are patentable over Gerolymatos, Faour et al., Thombre, Gennaro, and Federal Registry, 1997 as modified by Federal Registry, 1999.

Conclusion

Applicants respectfully submit that the pending claims are now in form for allowance.

The Commissioner is hereby authorized to charge any fee deficiency or credit any overpayment in connection with this amendment to Deposit Account No. 50-4260.

Respectfully submitted,

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